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EDITORIAL

SICK-BED READING

"There are many times when it is incumbent on the wise physician to prescribe not a posset or a purgative, but an essay or a poem." Such is the suggestion offered by a writer in a recent article upon the subject of literature in medicine. In our association, with this scientific era of medicine, we are apt to forget some of the more common-place aids in the practice of the art of medicine. One of these is the value of reading to the patient confined in bed, be it for short or long periods. Such reading should not necessarily aim at ultimate cultural effect, rather it should attempt to add some slight enjoyment to the enforced inactivity of the patient. Dr. Johnson's statement that all reading should be for pleasure is certainly more than true in the case of the bed-ridden.

A physician may well supplement his medicaments with a good book or books to hasten the recovery of the patient by giving him a certain tranquillity of mind which will aid him in his combat of the disease. In the choice of books the doctor may be of assistance if he knows the temperament of the patient and has a knowledge of suitable literature. Different patients will need different books, and all books cannot be counted on to affect all patients in the same way. One should aim to present to the patient books which neither depress unduly or excite alarmingly, but rather ones which will give the patient much to think about, but not too much about which to become emotionally upset. Biographies offer a most suitable

form of "literary prescription" for a patient. A patient may become particularly interested in the life history of medical men, while they themselves are suffering from an illness; in this connection it might appeal to some to read the life of Pasteur, Osler, and others.

Short stories are most popular with those who cannot concentrate for long without tiring, and do not desire "heavy" reading. One might even recommend a detective story if such is indicated. However, for the chronic case, a mixed selection is probably best and provocative of best results. It is in these cases in which the stay in bed is prolonged that the greatest benefits of books is seen; they serve to keep the patient cheerful, and shorten to him the otherwise long and dreary hours.

SEVEN WONDERS OF MEDICINE.

It was recently stated by Dr. B. C. Crowell, Associate Director of the American College of Surgeons, that the following are the seven wonders of modern medicine:

1. Immunity or resistance to disease.
2. Anaesthesia and analgesia, giving relief from pain.
3. Antisepsis and asepsis, preventing wound infection.
4. Vitamins and food values.
5. Light and ventilation.
6. Organotherapy, such as feeding liver in pernicious anaemia, giving insulin in diabetes, and thyroid gland to hypothyroids.
7. Periodical health examinations to prevent the effects of certain diseases, such as cancer.

Knowledge of these "seven wonders" has been available to the medical profession only for the last fifty years, and it is these means with which the modern physician combats disease in the main. How different is the study of medicine now as compared with one or two generations ago?

KETOGENIC DIET IN PYELITIS.

Helmholtz has recently announced an advance in the treatment of chronic pyelitis. His contribution is the application of the ketogenic diet in these cases for the purpose of increasing the acidity of the urine beyond what may be obtained by the use of drugs. He cites several cases in which a chronic pyelitis of months or years' standing has been cleared up in as short a time as ten days.

The discovery of this effect of a ketogenic diet came about in a most interesting manner. During some work with epileptic patients to whom a ketogenic diet was being given, it was noted that their urine, even if left a long time, did not show bacterial growth and the changes occurring in normal urine upon standing. This discovery led to the trial of the diet in cases of chronic pyelitis, with apparently spectacular results.

RESUSCITATION AFTER ELECTRIC SHOCK

By WILLS MACLACHLAN, HYDRO ELECTRIC POWER COMMISSION.

Respiratory failure due to drowning has come down through the ages and to this condition, two additional emergencies partially due to our industrial civilization, have been added, siz.: Electrical shock and carbon monoxide poisoning. In each of these emergencies assistance by trained persons must be given at once if the patient is to survive.

The electrical public utilities have for years been fully aware of this condition, and have studied the situation, assisted in research of a fundamental character, and have had their employees instructed and trained in applying remedial measures. Over 500 persons have been resuscitated from electrical shock in the last ten years by employees of electrical public utilities in Canada and the United States. For these reasons the public utilities welcome the opportunity of placing certain facts in connection with electrical shock before the medical profession, and of demonstrating the knowledge of employees in remedial measures. This opportunity is also welcomed as a means of acquainting the doctor, who may be called to a case being handled by employees of public utilities, with what he may expect these employees to be doing when he arrives, and with the instructions they have received as to the handling of the case.

An electric shock is usually received by inadvertently allowing an electrical current to pass through the body. Usually this is caused by bringing one hand, the back of the neck, the shoulder or elbow in contact with an energized conductor and either standing on ground or having the feet or lower part of the body in contact with metal wires or pipes (such as plumbing) connected to the ground. As one side of most electrical circuits is solidly connected to the ground for protection of life and property, the victim really places his body across the circuit. In a few cases, contact is made between two energized wires.

The severity of the shock is increased if the part of the body or clothing in contact with the wire or ground is wet, as the contact resistance is decreased; hence fatalities in bathrooms. The severity of the shock is also increased if the passage of the current through the body is prolonged, such as for a few seconds.

The immediate effect of the passage of a current of electricity through the body is a paresis or disturbance of all of the higher centres and a tonic spasm of the muscles. This results in:

1. Respiratory failure from paresis of the respiratory centre.
2. A disturbance of the heart, as yet not clearly understood.
3. Paresis of the vasomotor system.
4. Unconsciousness.
5. Negative eye reflex and failure of other reflexes.

The treatment indicated is the immediate application of the Prone Pressure Method of Artificial Respiration by well trained men. To this is added the application of heat by blankets and hot water bottles. The use of hypodermic stimulants, as well as oxygen, or oxygen and carbon dioxide in laboratory animals was fruitless for electrical shock, and such are not to be recommended at present in field cases of electrical shock. Further laboratory work in this direction is in hand.

In view of the fact that the eye reflex and other reflexes are negative, the employees of public utilities are instructed to carry out resuscitation until the patient breathes or there are definite signs of the onset of rigor mor-

tis. This instruction is paraphrasing Jex Blake in the British Medical Journal of March 15th, 1913. In one case, May 20th, 1927, a young man received a shock of 26,000 volts from back of head to hands and feet at 2 p.m. Artificial respiration was immediately started and continued with relays of men until the man was breathing of his own volition at 10 p.m., eight hours of resuscitation to success.

The men are trained to change from one operator to the next without losing a stroke and without losing the rhythm. After the patient starts breathing, the men are instructed that he must be kept lying down and not be allowed to stand or to sit up because of the paresis of the vasomotor system. He is to be transported in a lying down position to his home or hospital, put to bed and treated as for surgical shock. Warmth, rest, quiet, etc. Unnecessarily long transportation is to be avoided. It is much better to bring the necessary parts of the hospital to the man than the man to the hospital.

The men receive instruction in elementary physiology, so that they have some knowledge of the "Why" as well as the "How" of resuscitation. They are then trained in artificial respiration according to the Prone Pressure Method first put forward by Sir Edward Sharpey Schafer. This training includes both acting as an operator and as a patient. They are then required to practise at least once a month and records of practices are kept. Some gangs practise once a week. Their proficiency is therefore maintained at a high level.

At the time of an electrical accident in which the men of the electrical public utilities are involved, telephone communication is established with headquarters and consulting advice is available.

To recapitulate:

1. Clear the victim from current as quickly as possible; seconds count.
2. Start resuscitation by prone pressure method, by well-trained men, as quickly as possible.
3. Use warmth, blankets, hot water bottles, etc.
4. Carry out resuscitation until patient breathes or there are definite signs of the onset of rigor mortis.
5. After the patient is breathing of his own volition, do not allow him to sit or stand, but transport in a lying position to home or hospital, and put him to bed and treat as for surgical shock.

The method outlined is also applicable in cases of drowning and gas poisoning.

INSTRUCTIONS FOR RESUSCITATION.

I.—Free the Victim from the Circuit Immediately.

1.—Quickly release victim from current, being careful to avoid receiving a shock. Use any dry non-conductor (rubber gloves, clothes, wood, rope, etc.) to remove either victim or conductor. Beware of using metal or any moist material. If necessary shut off current.

2.—As soon as victim is clear of conductor, rapidly feel with your finger in his mouth and throat and remove any foreign body (tobacco, false teeth, etc). If mouth is tight shut, pay no more attention to it until later. Do not stop to loosen patient's clothing, but immediately begin actual resuscitation. Every moment of delay is serious. Proceed as follows:

II.—Instantly Attend To Victim's Breathing.

1.—Lay the patient on his belly, one arm extended directly overhead, the other arm bent at elbow and with the face turned outward and resting on hand and forearm, so that the nose and mouth are free for breathing (see Fig. 1).

2.—Kneel straddling the patient's thighs with your knees placed at such a distance from the hip bones as will allow you to assume the position shown in Fig. 1.

Place the palms of the hands on the small of the back with fingers resting on the ribs, the little finger just touching the lowest rib, with the thumb and fingers in a natural position, and the tips of the fingers just out of sight (see Fig. 1).

3.—With arms held straight, swing forward slowly so that the weight of your body is gradually brought to bear upon the patient. The shoulder should be directly over the heel of the hand at the end of the forward swing (see Fig. 2). Do not bend your elbows. This operation should take about two seconds.

4.—Now immediately swing backward so as to completely remove the pressure (see Fig. 3).

5.—After two seconds swing forward again. Thus repeat deliberately twelve to fifteen times a minute the double movement of compression and release, a complete respiration in four or five seconds.

6.—Continue artificial respiration without interruption until natural breathing is restored, if necessary, four hours or longer, or until a physician declares the patient is dead.

7.—As soon as this artificial respiration has been started, and while it is being continued, an assistant should loosen any tight clothing about the patient's neck, chest or waist. KEEP THE PATIENT WARM. Do not give any liquids whatever by mouth until the patient is fully conscious.

8.—To avoid strain on the heart when the patient revives, he should be kept lying down and not allowed to stand or sit up. If the doctor has not arrived by the time the patient has revived, he should be given some stimulant, such as one teaspoonful of aromatic spirits of ammonia in a small glass of water, or a hot drink of coffee or tea, etc. The patient should be kept warm.

9.—Resuscitation should be carried on at the nearest possible point to where

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA.

The Royal College of Physicians and Surgeons of Canada desires to announce that the Annual Primary and Final Examinations for Fellowship in the College will be held in Montreal, October 9th to 14th, 1933.

Candidates desiring information with reference to examinations for the Diploma of Fellow are requested to communicate with the Honorary Secretary, Royal College of Physicians and Surgeons of Canada, Dr. Warren S. Lyman, 292 Somerset Street, Ottawa.

Fig. 1. Position in which patient should always be placed and kept until conscious; also first position for operator starting artificial respiration.

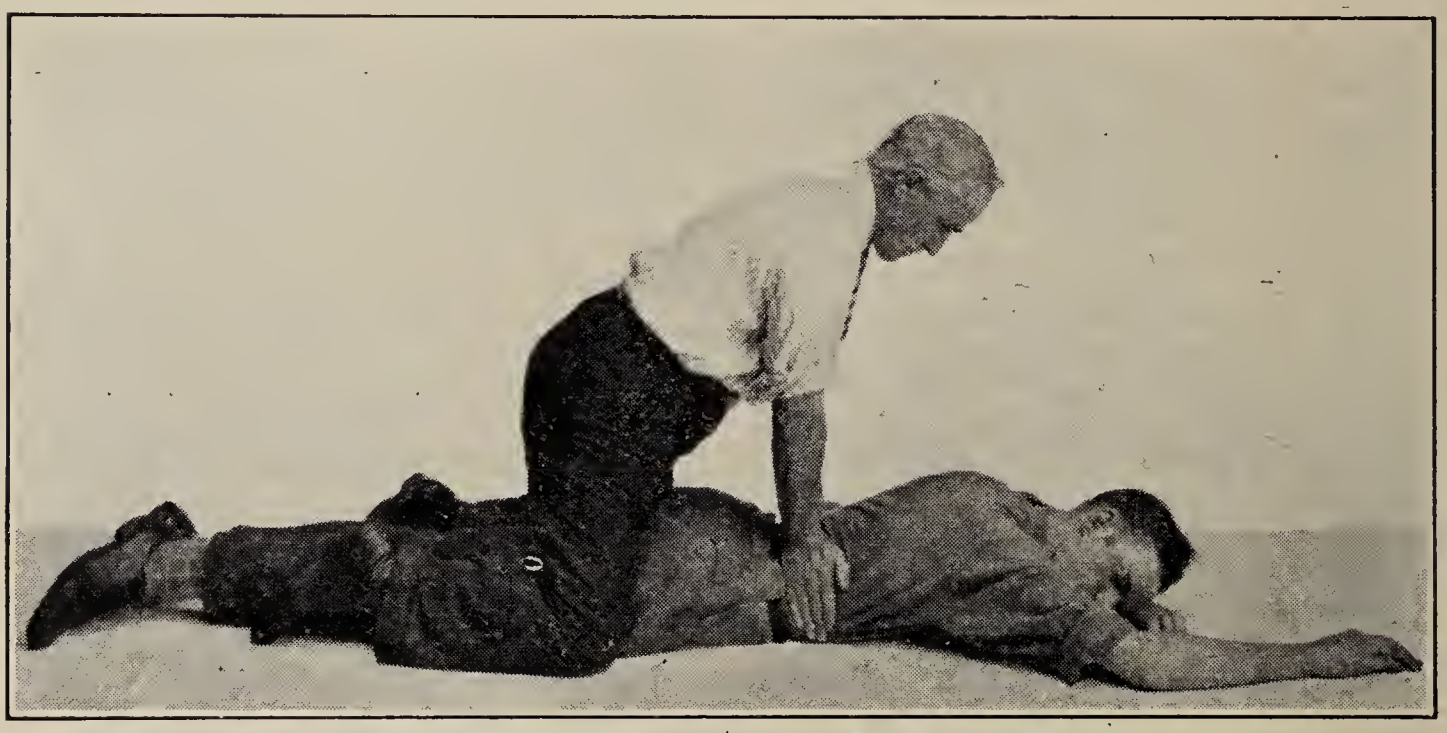

Fig. 2. Second position of operator giving artificial respiration.

Fig. 3. Third position of operator giving artificial respiration.

the patient received his injuries. He should not be moved from this point until he is breathing normally of his own volition, and then moved only in a lying position. Should it be necessary, due to extreme weather conditions, etc., to move the patient before he is breathing normally, resuscitation should be carried on during the time that he is being moved.

10.—A brief return to natural respiration is not a certain indication for stopping the resuscitation. Not infrequently the patient after a temporary recovery of respiration stops breathing again. The patient must be watched, and if natural breathing stops, artificial respiration should be resumed at once.

11.—In carrying out resuscitation, it may be necessary to change the operator. This change must be made without losing the rhythm of respiration. By this procedure no confusion results at the time of the change of operator and a regular rhythm is kept up.

III.—Send For Doctor.

If alone with victim, do not neglect immediate and continued resuscitation in order to call a doctor. Start at once—the first few minutes are valuable. If other persons are present, send one of them for a doctor without a moment's delay.

The ordinary and general tests for death should not be accepted, and any doctor should make several very careful and final examinations and be sure specific evidence is present before pronouncing the patient dead.

In view of the careful and extensive experiments carried out under Professor Macleod's direction, a statement from him is extremely important.

Paralysis of the nerve centre which controls breathing is the cause of death in many cases of electrocution, and, provided the heart has not been directly affected by the current, natural breathing can often be restored by artificial respiration. This allows the still circulating blood to be aerated in the lungs. The only method to employ is Schafer's Prone Pressure Method and a pulmotor or any other form of apparatus should never be used. Since the paralysis of the breathing may last some time, it is necessary to continue artificial respiration sometimes for hours, and it should never be discontinued until it is absolutely certain that the heart has ceased beating. As far as can be judged by observations on electrocuted animals, no advantage is gained by using oxygen or carbon dioxide during the artificial respiration, or by administering heart stimulants. It is important to see that the body is kept warm. After natural breathing returns the patient must be kept lying down and he must be carefully watched for several hours to see that the paralysis of breathing does not return. If it does so, artificial respiration must be reapplied.

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GASTRIC EVACUATION

By MALCOLM WILSON, M.D., F.R.C.P. (C).

It is useless to consider the passage of food stuffs or other materials through the pyloric sphincter until we understand how they transverse the stomach to reach the sphincter. All liquids pass rapidly along the lesser curvature of the stomach and attain the region of the pyloric antrum almost immediately. On the other hand, a solid meal may take half an hour or more to reach the sphincter. We can therefore state that in normal individuals the passage through the stomach depends on the consistency of the material ingested.

In one series of experiments several substances of no food value were ingested by four normal young men. These "meals" were each of 240 ccs. total volume, and each contained 40-gms. of barium sulphate, which was intimately mixed with the material to be investigated. All the substances were finely divided. The meals were consumed after fasting for five or six hours to be sure that the stomach was empty. Fluoroscopic observations were made of the meal on traversing the stomach, of the initial passage of material into the duodenum, of the depth of peristaltic waves, and of the percentage which remained in the stomach at 1½, 3 and 4½ hours after the commencement of ingestion of the meal. The method of investigation is exact as to the initial evacuation of the stomach, but is only approximate for the observations of percentages in the stomach at subsequent periods, for the reason that these depend on estimates. This error was minimized as far as possible by having all the estimates made by one man, and all were checked by another.

The results in one subject are given in Table 1. Four substances having practically no food value were given. By comparing Column 2 with Column 1, it will be seen that the time taken to leave the stomach is roughly comparable to the time taken in swallowing. (All meals were ingested as rapidly as possible). In the last three columns are shown the percentage of the meal which has left the stomach at the times stated, and it will be obvious at once that both the first emptying of the stomach and the subsequent rate of evacuation are dependent upon the consistency of the material ingested.

It should be remembered that the consistency of some foods changes in the stomach due not only to the secretion of gastric juices, but also to their partial digestion. The substances listed above, as far as is known, do not excite any considerable secretion, and

TABLE I.

Gastric Evacuation — Substances of No Food Value.

	Minutes to swallow	First leaving of stomach (minutes)	Percentage out of stomach in 1½ hrs.	3 hrs.	4½ hrs.
Liquid paraffin	1	2	80	100	..
Agar jelly	5	19	40	65	85
Cabbage, ground	2	25	25	60	70
Bran, washed	12	90 (plus)	0	20	35

TABLE II.

Gastric Evacuation — Various Foods.

	Minutes to swallow.	First leaving of stomach (minutes)	Percentage out of stomach in		
			1½ hrs.	3 hrs.	4½ hrs.
Carbohydrates:—					
Thick porridge	2	4	75	95	..
Bread 40 gm. Dates 100 gm	3	3	60	95	..
Proteins:—					
Egg white, raw	1	3	75	85	90
Codfish, boiled	5	20	30	85	95
Lean meat, baked	5	7	40	80	90
Fats:—					
Cream 32 p.c.	1	1	25	40	70
Bacon and egg yolk	5	12	10	30	95
Olive oil	1	1	25	50	60

their consistencies are not changed by digestion in the stomach.

In the second series of experiments on the same subject, a number of foods were investigated. All of these were finely divided. For example, raw egg white was rubbed through a sieve and the lean meat was put through a meat chopper. The reason for this is that London showed in dogs that large lumps of meat left the stomach much more slowly than minced meat.

Table 2 shows the results obtained. A study of this Table will show that carbohydrates leave the stomach rapidly, that proteins are a little slower, and that fats are slowest of all. This is in agreement with the results of other workers using widely different methods of investigation.

When we come to study the reason for the slow evacuation of fats, we must first consider the forces which cause this evacuation. Nothing left the stomach in any of these experiments except in advance of a peristaltic wave. Peristalsis of the stomach is the only force concerned in the emptying of this viscus. It is true that gravity plays some part, because if a man lies on his left side, gastric emptying is much slower than if he lies on his right. In all the experiments here recorded, however, the subject was standing or sitting during the whole period. The only other force which has been suggested in this connection is a tonic contraction of the whole of the stomach, which would tend to force the contents through the sphincter. That this factor is of no importance is shown by the demonstration that in two subjects barium meals left the stomach in normal fashion while the pressure in the fundus was subatmospheric.

The peristaltic waves were deep at first in all cases, and with carbonhydrates they remained deep until the stomach was empty. In the case of fats, however, after five or ten minutes the peristaltic waves became definitely more shallow than at first, and remained so during the rest of the experiment. Thomas found that the waves were shallow in the case of proteins also. The reason for this reduction in peristaltic activity is at present not clear, but probably depends either on reflex inhibition from the small intestine, or on a humoral mechanism due to the circulation in the blood of some of the products of digestion.

From the above results, we can now state that after the commencement of gastric evacuation its rate depends on two factors, the consistency of the gastric contents and the vigour of the peristaltic waves.

Peristaltic activity of the stomach is influenced by a great variety of factors. The common cold, for example, decreases peristalsis. The same is true of any other infection. Deep anaesthesia abolishes the waves completely. Violent exercise stops peristalsis for five or ten minutes or even longer after the exercise has ceased. Mild emotions increase the depth of the waves, but violent emotions depress them. Mild irritation of the colon increases peristalsis, but, if severe, has the opposite effect. Severe pain or shock causes cessation of all waves. Peristaltic activity is increased by the administration of alcohol, coffee, strychnine, histamine, insulin or choline chloride, and is depressed by smoking, atropine, ephedrine, codeine, vitamin B deficiency and the inhalation of amyl nitrite. Morphine increases peristalsis for twenty minutes or half an hour, but subsequently depresses it for a long period.

Thus we see that gastric evacuation in normal human beings is dependent only on the consistency of the gastric contents and on peristaltic activity but that both may vary widely. The consistency of the gastric contents is altered by the secretion of gastric juice and by the partial digestion of the food. The vigour of peristalsis is affected by mental and physical activity, by many of the things we eat and drink, and by very many drugs.

CARCINOID TUMOR OF THE APPENDIX*

By PAYSON B. AYRES, M.D.

Pathology.

Appendicular carcinoids may be discovered by chance in routine autopsy examinations and in routine surgical sections of the appendix (.3% — .4%) where no abnormal pathology is suspected, or they may be observed in surgical specimens removed for clinical manifestations; which are usually those of subacute or chronic appendicitis.

The common site for this tumor is in the tip of the appendix (90%), where it may be microscopic or macroscopic in size, the largest tumor on record being about the size of a pigeon's egg. When accompanied by symptoms with no other pathology in the appendix, the condition is usually considered clinically to be that of a sub-acute appendicitis. The tumor, however, may be found anywhere in the body of the appendix, where to produce clinical manifestations it must be of a size sufficient either partially or completely to occlude the lumen. Masson, however, claims that even in small tumors the accompanying periglandular neural hyperplasia may be responsible for the indications of disease in the appendix. If complete occlusion is the case, acute inflammation is generally present. If partial occlusion is present, the symptoms may or may not be those of subacute or chronic disease. A slight swelling of the appendix may be the only evidence of the tumor, or it may be evidenced by a yellowish infiltration of the overlying peritoneum and the adjacent peritoneal fat.

On section, the tumor has a yellowish or brownish appearance, is hard to the touch, and is found as a definite localized mass with no true capsule. There is usually no evidence of lumen in the appendix, fibrous connective tissue having replaced the mucosa, and the tumor being found growing from the inside of the appendix outward.

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*Part of a sixth year Thesis for Dept. of Pathology, 1932.

Differentiation Of Carcinomata And Carcinoids.

Although carcinoids bear a microscopic resemblance to the carcinomata, they have long been classed as clinically benign. This resemblance is morphological and it ends there; moreover, if the observer searches his slide of the carcinoid tumor carefully,, he will find no evidence of the mitotic figures so often seen in the malignant growths. Although a few investigators have reported metastatic carcinoids, this is the exception rather than the rule, and while it must be admitted that any cell is subject to the laws of malignant change, evidence is overwhelmingly in favor of the benignity of this form of tumor. However, multiple carcinoids are often observed. Further, the presence of capillaries, venules and lymph spaces lying between the cell nests of the carcinoids are never subject to invasion or destruction at the hands of the tumor cells. While it is true that the carcinoid cells may and do break through the ensheathing muscularis mucosae, penetrate the muscle, and even invade the peritoneal fat, they stop there, and do not infiltrate surrounding structures. No red cells are ever seen lying next these cells, and necrosis and cyst formation in the columns are not observed, as is so often the case where malignant growths are concerned.

It must, however, be borne in mind that the mucosa of the appendix is subject to malignant change, similar to that seen throughout the intestinal mucosa, and true carcinomata of the appendix do occur, with findings clinically and pathologically identical with those seen in carcinomata elsewhere in the gastro-intestinal tract. It is important to remember this and distinguish between the two types of tumor. The part played by chronic irritation in the production of carcinomata may be brought forward to explain the origin of the carcinoid and the close association of inflammation with the presence of the growth is an observation we have already made. It may be argued, hence, that this may be a precancerous change, but later we hope to show, in the section on the origin of the carcinoid, that such is not the case.

Apparently, then, the carcinoid produces no symptoms of itself — and although it may cause obstruction, the inflammatory reaction to the ensuing infection produces the symptoms. Were there no complications then, following the growth of the tumors, we may suppose they would never manifest themselves, and from the number of carcinoids found during laparotomies and autopsies whose presence was never suspected, such seems to be the case.

Histology.

The typical picture seen in the microscope is that of nests and columns of epithelial cells, varying in length and breadth, usually seen in the submucosa. The cells are usually spheroidal in shape, with deep staining nuclei and a pale granular cytoplasm. There may be vacuoles in some of the cells, and these cells are often gathered in a pseudo-glandular arrangement. The supporting stroma is fibrous connective tissue in which smooth muscle cells may be found in varying proportions. Blood vessels and lymph spaces may be found between the cords. There is no stroma supporting each cell, the cells as a rule being loosely packed. As before mentioned, while occurring chiefly in the submucosa, the cells may penetrate through the muscular coats and reach the serosa, by displacing the muscle cells. No destruction or necrosis of muscle is evident, the cells lying between the muscle fibres. Red cells are never found lying loose next the tumor cells.

While the spheroidal cell is the commonest, palisade and columnar cells have been described, each with the following characteristics:

The round cells have central, round and turgid nuclei, the network is finely reticulated and contains numerous chromatic granules. The cytoplasm

may be of an even consistency or it may contain many granules, both staining acidophilically. There may be fine vacuoles in the cells.

Palisade cells are also found having nuclei similar to those of the round cells. These cells are found mixed in the columns with the spheroidal variety, and lie next the connective tissue. The nucleus, however, is separated from the base of the cell by some distance in which many acidophile granules are found. In these cells the vacuoles usually appear above the granules supranuclearly. When compressed or when crowded these cells may assume a tense rigid form, with a slim base bordering on the connective tissue.

The third type of cells is described as columnar, and comprises those which form the pseudo - glands seen in this tumor. They are found in rosette form around a small cavity which may contain a drop of material resembling colloid. The nucleus is similar to that of the others and is found in the middle of the cell. The apical pole is clear or vacuplated and presents to the cavity, while the base of the cell is loaded with granules and rests on the surrounding connective tissue. These three cells have, as a rule, definite cell membranes, the last two resting on the surrounding connective tissue, the cells apparently utilizing this as a basement membrane. The connective tissue stroma may contain such a quantity of smooth muscle cells that the tumor resembles a myoma. As has been mentioned, these muscle cells apparently originate from the muscularis mucosae, certain investigators having found them growing up between the tumor cells from this thin layer of muscle.

History of the Carcinoid: Its Structure and Development.

The first tumor of the appendix reported in literature was noted in 1834 by Merling. Subsequent to that, several observers noted carcinomata of the appendix and described them, but it was not until 1888 that any contribution was made toward the subject in hand. Lubarsch in that year reported two cases in which small, white nodules were found in the ileum lying in the submucosa and in the muscularis. These nodules on section were found to be composed of tumor cells which differed greatly from the cylindrical cells that form the adeno carcinoma of the gastro-intestinal tract. Serial section seemed to show a connection between these cells and the crypts of Lieberkuhn, and Lubarsch suggested that these were probably outgrowths from the glands of the mucosa. He described cells that we now call carcinoid, and also noted that they occurred in a pseudo-glandlike formation at times. He further made the following observations in regard to these growths:

(1) That the tumor growths are multiple.
(2) No metastases are found in connection with them.
(3) No true gland structures are contained in the tumors.
(4) The cells are unlike those of the normal intestinal mucosa.

Even with these accurate observations, he was content to call them "primary carcinoma of the ileum."

Following Lubarsch, Ransom in 1890 recorded a case of a tumor of the ileum which extended through the intestinal coats, through the peritoneum, and invaded the mesentery. Microscopical features of this tumor resembled those reported by Lubarsch, but Ransom found multiple metastases in the liver, and hence concluded the tumor was malignant in character.

Later, in 1896, Notthaft described tumors similar to Ransom's, which also showed metastases. These observations seemed to show that the tumor was a true carcinoma Just before Notthaft's report, Glazebrook described a tumor whose characteristics resembled those of Lubrasch, which was as large as a filbert nut, and was found in the appendix. In this case, however, no extensions or metastases were found.

Glazebrook, however, thought that the spaces in the tumor were blood vessels or lymphatic spaces, and hence deducted that it was endothelial in origin, and gave it the name of "endothelial sarcoma."

In 1903, Elting made a comprehensive review of the early literature, and in all the tumors of this type listed, found that twenty-three of them were reported as arising in the appendix. The first step, rather mis-step, towards solving the mystery of the origin of this neoplasm was taken by Bunting in 1904, who pointed out that morphologically and biologically these tumors were similar to the basal-celled epithelioma previously described by Krompecher This suggestion was opposed by Oberndorfer in 1907, who clearly differentiated between this "primary carcinoma of the appendix" and carcinoma of the g.i. tract, and suggested they be given the name of carcinoid or carcinoma-like tumor, basing his contention on the following points:

(1) These tumors are often multiple.
(2) The cells largely consist of undifferentiated masses or may be glandular in form.
(3) The tumors are circumscribed and show no tendency to infiltrate surrounding tissues.
(4) The tumors do not metastasize.
(5) The tumors grow very slowly and never reach any great size.
(6) The tumors are always found in the submucosa.
(7) The tumors are always clinically harmless.
(8) The muscularis mucosae is always present and not broken down.
(9) The stroma is composed of smooth muscle.

In regard to this last observation, he demonstrated to his own satisfaction that the muscular stroma was connected with the muscularis mucosae directly, and hence was probably derived from the latter structure. Next, Trappe suggested that these tumors had their origin in pancreatic tissue rests, and that these rests might form either adenoyyoma or a carcinoid tumor, depending on certain unknown controlling factors. Following him, Burkhardt in 1909 contested Trappe's theory on the following grounds:

He claimed that the tumor differed from pancreatic tissue

(1) By the fact that no acini were ever found.
(2) That in pancreatic tissue there is never found a muscular stroma.
(3) That in the carcinoid tumor no ducts or duct-like structures were ever seen.
(4) That there was always a demonstrable connection between the tumor nests and the glands of Lieberkuhn.
(5) That pancreatic growths invaded surrounding tissues and produced metastases which the carcinoid tumor was never known to do.

Burkhardt, however, supported Bunting's hypothesis that these tumors were basal-celled on the following grounds:

(1) The tumors seemed to be derived directly from intestinal epithelium.
(2) They also were of low grade malignancy.
(3) They possessed a hyaline fibrous stroma.
(4) The cells were undifferentiated.

The following year, Toenniessen returned to the pancreatic rest theory, advancing the suggestion that submucous rests from the pancreas were responsible for the production of the carcinoid. In this connection, he claimed a similarity between the carcinoid cell and the cells of the islands of Langerhans.

This was further developed by Saltykow, who claimed that these submucous pancreatic cell rests produced only cells similar to those of the islands of Langerhans. It is in view of these theories that some little attention is paid later in this paper to differentiating between the carcinoid cell and other cells of the endocrine organs. About this time, Oberndorfer, pursuing his histological investigations of the carcinoid cell, reported a chrome reaction of the protoplasm, and demonstrated the presence of double refracting bodies in the cells. This is an important observation which we shall see developed later.

In the same year (1910), Hibschmann made the first productive suggestion when he noted a similarity of color between the "Gelbenzellen" of the intestinal mucosa and the yellow cells of the carcinoid tumor. He also tried to show a relation between the 'Gelbenzellen" and the Nicholas Kulchitsky cells, but did not arrive at any significant conclusion.

In 1914, Gosset and Masson, however, repeated the known investigations and made further important and extensive studies of the Nicholas Kulchitsky cell. Being struck with their chrome reaction, they used an ammoniacal silver stain and succeeded in demonstrating the Nicholas Kulchitsky cells in the intestinal mucosa. These two observers have, since that time, contributed most in this field, although Komprecher in 1919 tried to supplement his previous observations, but was unable to bring forth conclusive proof that carcinoids were related to basal-celled carcinomata.

Conclusion.

(1) The carcinoid tumor is composed of argentaffin cells almost identical in morphology and content with the argentaffin cell found in the submucous neuromata of the appendix. The argentaffin cells of these neuromata are derived by budding and migration from the Nicholas Kulchitsky or chromo argentaffin cell in the glands of Lieberkuhn found in the appendicular mucosa. Hence the carcinoid tumor cell is in reality identical with the Nicholas Kulchitsky cell of the intestinal mucosa.

(2) The carcinoid tumor cell may have two functions. Morphologically it gives evidence of an endo and exocrine function.

(3) The carcinoid tumor cell is not malignant, as evidenced by its origin, development and clinical course. The carcinoid tumor cell may or may not be associated with pathological findings in the appendix. The development of the carcinoid tumor is influenced by certain conditions, two of which may be:

(a) The stimulus of non-macerating inflammation in the appendix, coupled with

(b) An active period of neuro-genesis.

(4) Special stains and prolonged searches are necessary to trace the origin and development of this tumor.

ARTERIAL DISEASES OF THE EXTREMITIES

I. PATHOLOGY AND AETIOLOGY.

By J. C. RICHARDSON, M.D.

In recent years a great deal of interest has been shown in this subject, stimulated by the work of Royle, Hunter, Leriche and others, on the surgery of the sympathetic nervous system. In considering this method of improving the circulation to an extremity, it is, of course, necessary to know the nature of the underlying arterial lesion. The following is a review of our present knowledge of certain occlusive arterial diseases of the limbs considered under the headings of aetiology and pathology, with some historical notes.

1. Clinical Classification.

Let us first, for the sake of completeness, attempt to classify all the arterial diseases of the extremities. This is very difficult to do, but the following classification by Brown, Allen and Mahorner, is probably as accurate a grouping as possible at present on any rational basis:—

CLINICAL CLASSIFICATION.

Arterial Vascular Diseases—Brown, Allen and Mahorner.

1. Functional or Vasomotor Types
   - a. Local Distribution
     - (1) Vasoconstricting Types
       - (i) Multiple Phase Colour Reaction — Raynaud's Disease.
       - (ii) One Phase Colour Reaction — Acrocyanosis — Dead Finger —Local Syncope.
     - (2) Vasodilating Types—Erythromelalgia.
   - b. General Distribution
     - (1) Vasoconstricting—Primary or Essential Hypertension.
     - (2) Vasodilating—Primary or Essential Hypotension.
2. Organic Types
   - a. Local Distribution
     - (1) Arteriosclerosis, with or without gangrene,—diabetic gangrene.
     - (2) Thrombo-angiitis Obliterans.
     - (3) Simple Thrombosis or Embolism.
     - (4) Arteritis of Known Infectious Origin.
     - (5) Aneurysm with or without Thrombosis.
   - b. General Distribution
     - Arteriosclerosis
       - Primary.
       - Secondary—lead, etc.

II. Aetiology and Pathology.

The diseases to be discussed in detail are three arterial diseases of the extremities which are associated with narrowing or occlusion of the lumina, namely, Arteriosclerosis, Thrombo-angiitis Obliterans, and Raynaud's disease.

"A." Arteriosclerosis In The Extremities.

(i) Definition—It is impossible to define the word "arteriosclerosis" satisfactorily as the aetiology is not fully known, and, moreover, the term is not a specific one. As introduced by Lobstein in 1835, it means a hardening and thickening of the arteries, as determined clinically, irrespective of the cause. The common arteriosclerotic lesion in the extremities is the Monckeberg type of sclerosis, which is a degeneration and calcification in the muscular media of the arteries. In some cases a stenosing endarteritis occurs which may be followed by occluding thrombosis. Such cases will show evidences of circulatory impairment.

(ii) Historical Note—The relation of gangrene to the blocking of vessels was recognized by Boerhaave, Munro and Meckel. The early writers of the

nineteenth century paid special attention to diseases of the arteries, and Hodgson's excellent monograph appeared in 1815. Virchow's study of the disease, which he called "endarteritis deformans," brought out its relation to strain, increased pressure and toxic agents. The view of arteriosclerosis as a general disease dates from the papers of Gull and Sutton, 1872.

(iii) Aetiology—Factors known to contribute to the production of this sclerosis are old age, work, diabetes and hypertension. Other unknown factors, such as infections and intoxications, must undoubtedly play a part.

Ninety per cent. of cases occur in the age group 50-85 years, the lesion being found uncommonly at somewhat younger ages. Certain retrogressive changes occur in the arteries of all individuals with advancing age. Loss of elasticity occurs, and there is atrophy and loss of substance of muscle tissue. Klotz states that arteriosclerosis as we see it clinically and in the laboratory, is an acquired condition and should not be confused with these physiological changes. Progressive degenerative changes have occurred in the Monckeberg sclerosis and Endarteritis Obliterans of such degree to suggest that added factors must have been present, as well as the normal wear and tear of life.

Monckeberg's sclerosis seems to bear a definite relation to muscular work. It is more marked in the manual labourer, and has been shown to be more advanced in the right arm of right-handed individuals.

Arteriosclerosis in its various forms is now one of the most feared complications of diabetes. Warren, in a series of 300 diabetic autopsies, states that there was no case of diabetes of more than five years standing which did not present some arteriosclerosis. Monckeberg's arteriosclerosis frequently occurs under forty years of age in diabetes, and Joslin reports nine cases showing calcification in children. Various explanations have been offered for the development of arteriosclerosis in diabetics. It has been attributed to hyperlipemia, infections and deficient glycogen storage in the smooth muscle of the arteries.

Continued high blood pressure is commonly associated with arteriosclerosis in various forms. It does not predispose to any one particular type of arterial lesion.

Stopford has suggested recently that prolonged spasm of arteries by irritation of sympathetic nerves can produce medial degeneration, intimal changes and thrombosis, possibly by constriction of the vasa vasorum. This explanation might have some bearing on the usual lesion of the peripheral arteries, and may explain the production of medial degeneration experimentally by vaso-constrictor drugs.

Vanderveer working on rabbits reports hypervitaminosis D produces calcium deposits about the elastic fibres of the media and later some degeneration of muscle cells.

(iv.) Pathology. — Arteries of the extremities amputated for gangrene due to arteriosclerosis, will show besides the usual Monckeberg lesion of the media, considerable intimal thickening spoken of as Endarteritis Obliterans, and thrombus formation. The following description is of such arteries.

(a) Gross Appearance.—In the upper extremity the radial and ulnar arteries are most commonly involved, the brachial less frequently. In the lower extremity, the arteries involved are in order of frequency: anterior tibial, posterior tibial, popliteal and femoral. The affected vessels appear as rigid, inelastic tubes collapsible only in uninvolved portions. Hard plaques or complete rings of calcium may be felt in the walls. The artery is often quite tortuous. There is no adherence of artery, vein and nerve as in Buerger's disease. On opening the vessel, the lumen, where patent may be normal or larger in size. In other areas, irregular encroachments on the lumen oc-

cur as gross evidence of intimal thickening. In some regions the arteries are completely occluded by a pearly yellow gelatinous material or by a fresh reddish thrombus.

(b) Microscopic Appearance.—Certain degenerative and proliferative changes are seen in the different coats of the artery.

The adventitia is characterized in this disease by almost complete absence of lesions. There is no cellular infiltration, fibrosis or vascular change. Elastic fibres may be increased in number.

The media shows definite retrogressive changes. Interstitial connective tissue and elastic fibres are increased. There may be mild infiltration of lymphocytes. Definite blocks or complete rings of calcium are present in the inner part of the media, some of which may present bony metaplasia. New vascular channels occur as large sinuses.—(Monckeberg lesion).

The internal elastic lamina which normally appears as a clearly outlined regular way band of elastic fibres, is distorted and split.

The intima shows definite thickening. In cross section of the artery this may appear as a crescentic encroachment of the lumen, or as a diffusely thickened ring. The intimal cells are degenerated, the cell outlines being indistinct and the nuclei pale-staining. Hyaline or fatty degeneration may be present, producing a homogeneous, glazed, eosin-staining tissue.—(Endarteritis Obliterans).

Considerable narrowing of the lumen may be present due to endarteritis, but complete occlusion is usually preceded by thrombosis. Section through an occluded vessel shows a central thrombus in varying degrees of organization and recanalization.

(v.) Effect on the Circulation.—The common arteriosclerotic lesion of the extremities, namely, degeneration and calcification of the media, does not produce narrowing of the lumen per se. but, the rigid inelastic vessel is unable to regulate the blood supply in accordance with the needs of the tissues. Endarteritis occurs in vessels already showing Monckeberg's sclerosis in the media. When occlusion does occur from endarteritis and thrombosis, the rigid anastomatic arteries are unable to dilate to provide the maximum collateral circulation. As a result, there usually develops a dry gangrene or mumification in the extremity.

(vi.) Arteriosclerosis and Gangrene of the Extremities in Diabetics.—The type of arteriosclerosis of peripheral vessels in diabetics is the same as in non-diabetics. McKittrick and Root believe that there is a predominance of the endarteritis over the medial lesion. Because of existing metabolic deficiencies, gangrene is more prone to develop following trauma. The incidence of arteriosclerosis in its various forms, in diabetes, has greatly increased since the advent of insulin. Joslin's figures in 1930 show that arteriosclerosis now accounts for about 50% of diabetic deaths, whereas some thirty years ago, this figure was around 15%. This is probably due to two factors, (a) the decrease in the incidence of coma, and (b) the prolongation of life. As previously indicated, arteriosclerosis develops earlier in diabetics. Eliason and Wright in 100 cases of gangrene found that senile arteriosclerotic gangrene developed at an average of 64.9 years and diabetic gangrane developed at an average of 59.2 years. Average duration of life in sclerotic gangrene is much longer than in diabetic gangrene, so that it may be said that diabetic gangrene shortens life a full decade more than senile arteriosclerotic gangrene.

"B" Thrombo-angiitis Obliterans—Buerger's Disease.

(i.) Definition. — Thrombo-angiitis Obliterans may be defined as an organic lesion of the deep arteries and veins, and the superficial veins of the extrerities, characterized by an inflammatory process involving all three coats of the

vessels. This process is accompanied by an extensive occlusive thrombosis, which thrombus later becomes organized and vascularized.

(ii.) Historical Note.—Our knowledge of the pathology of this disease dates to the work of Von Winiwarter in 1879. He studied the vessels in an amputated leg in only one case, but his description and plates show undoubtedly that the disease he studied is that which we now call Thromboangiitis Obliterans. Buerger's investigation of a large number of cases marks an epoch in the study of the disease. His first paper, 1918, gives a new concept of the pathogenesis, and his book, 1924, gives a careful clinical and pathological study of the disease. He concluded that the lesion in an acute inflammation of the vessels going on to thrombosis and organization. Todyo studied five cases in 1912 and emphasized progressive mural thrombi in the pathogenesis.

(iii.) Aetiology.—The aetiological factors deserving consideration are age, sex, race, tobacco, focal and specific infection.

The age incidence is generally accepted as being 25-50 years. The disease occurs exclusively in males. Buerger diagnosed clinically three cases in females in a series of five hundred. One case in a female was pathologically diagnosed by Meleney and Miller, and this is the only verified case in the female reported. The limitation to the male sex might suggest a peculiar hereditary propagation as in Haemophilia. Various explanations have been suggested.

Buerger's report of 99% Hebrews in five hundred cases led to the belief that the disease was peculiar to this race. This view has been discarded since, as the disease has been reported in many other races. Ludlow recently reported that the disease occurs fairly commonly in Korea. In Brown, Allen and Mahorner's series 50% were Jews, which suggests a prevalence in that race. They suggest that reported racial predelection probably depends on the clientele of the investigator.

Tobacco was also stressed as an important aetiological factor by Buerger. There is some evidence that tobacco consumption is a contributing factor. Mayo and Silbert believe that tobacco plays an important role in causation.

Focal infection has been suggested as a factor. In 88 cases examined by Brown and Allen, only three were free from infection on teeth, tonsils or prostate

Nearly all observers have been impressed with the inflammatory appearance of the lesion, but no specific organism has been repeatedly isolated as yet. Rabinowitz isolated an organism from the blood of patients, with which he produced vascular lesions in rabits.

(iv.) Pathology.—The disease seems to occur almost exclusively in the vessels of the extremities. Buerger reports one case in the spermatic vessels, and Murphy a case in the renal vessels. The disease is four or five times more common in the lower extremity than in the upper. The condition is recognized as a progressive inflammatory process and the pathology shall be described in two stages, (i.) the early stage, and (ii.) the healed stage.

(a) Gross Appearance.—(i.) In the early or acute stage a definite thickening of the walls of the artery and vein is present, but the rigidity and inelasticity of the arteriosclerotic vessels are not found. Thrombosis occurs very early, more often in the artery than in the vein. Considerable lengths of the lumina may be seen to be occluded by a firm reddish and yellow thrombus. The vein may show nodules which, on opening the vessel, are found to be localized thrombi in the regions of the valves. (ii.) In the more advanced lesion, or the healed stage, there is seen a firm, dense, yellowish-white material completely occluding the lumen, converting the vessel into a fibrous cord. Pressure on the vessel may express a minute drop of blood from a

tiny canal in the occluding substance. There are no irregular encroachments on the lumen as in arteriosclerosis. The vessels are indurated and the vein, artery and nerve are bound together by tissue having the appearance of scar tissue.

(b) Microscopic Appearance. — (i.) The early stage. One of the earliest changes in the adventitia is the appearance of lymphocytes which are usually collected about the small vessels. The vasa vasorum may show increase in the number and size of the intimal endothelial cells and the lumina are larger than normal. The fixed connective tissue cells may show proliferative changes. The media may or may not show lymphocytes and polymorphonuclear leucocytes. The muscle cells are intact. Vessels appear in the media, which normally do not penetrate the media of the muscular type of arteries. In the intima, most observers note an active proliferation of the endothelial cells in arteries and veins. The thickened intima remains very cellular as in known inflammatory conditions. New vascular channels may appear in the intima and degenerative changes are absent. The internal elastic lamina remains as a definite wavy band. There may be a few lymphocytes between its fibres. The distorting and splitting of the arteriosclerotic lesion are not present. Thrombosis occurs very early and a dense mass of platelets and fibrin is seen completely occluding the lumen. The thrombus is infiltrated by many lymphocytes and possibly polymorphonuclear leucocytes. Beginning organization may be seen in the periphery by ingrowth of cells from the intima. Buerger describes "miliary giant-cell foci" in the periphery of the thrombus and interprets these as specific for this disease. After the periphery of the clot is well organized, ingrowing cells penetrate to the centre to form sinusoids. (ii.) Healed Stage. The pathogenesis of the earlier stages remains somewhat indefinite, but the finished result is well known to all observers. The adventitia presents very large vasa vasorum. Fibrosis may be marked. A few lymphocytes are usually seen. Marked increase in connective tissue is seen in all areas binding together the artery, vein and nerve. In the media, many new blood channels are seen. There may be slight degeneration of muscle fibres after prolonged occlusion, but this is usually absent. Fibrous tissue is increased between the muscle cells. The intima remains cellular and is well vascularized. The lumen is occluded by a cellular mass of connective tissue with occasional lymphocytes. Blood channels course through this tissue, some of which have three coats. Thus, vascular channels have increased by extension of vasa vasorum and formation of new vessels in all three coats and in the organized thrombus. This is evidently an attempt to establish collateral circulation and explains why the lesion may become healed without sufficient impairment of circulation to cause death of the tissues.

The same lesion occurs in the superficial veins as a Thrombo phlebitis, sometimes spoken of clinically as a Migrating Phlebitis. Buerger recognizes this in 20-25% of cases, Brown and Allen in 42%.

The change most common in nerves is an increase in perineural connective tissue, more marked where changes in associated vessels are more marked. This fibrosis is apparently due to the anatomical relation to the vessels. Occasionally, one sees extensive degeneration in the small nerves of the digit, believed to be due to a prolonged ischaemia.

It is generally agreed from pathological studies that Thrombo-angiitis Obliterans is an inflammatory disease. Buerger described acute inflammation with thrombosis as the primary lesion. Others, including Brown, Allen and Mahorner, conclude that the lesion is essentially a chronic inflammation. Klotz states that some cases show a definite acute inflammation with purulent giant cell foci as described by

Buerger, others show a subacute inflammatory reaction, and others a granulomatous type of lesion.

"C" Raynaud's Disease.

(i.) Definition.—Raynaud's Disease is defined by Osler as "A vascular change occurring without organic disease in the vessels, chiefly seen in the extremities, but also occurring in internal parts, in which a persistent ischaemia or passive hyperaemia leads to a disturbance of functions or to a loss of vitality with necrosis."

(ii.) History.—This affection is given the name of the distinguished French physician, Maurice Raynaud, because he gave it the best description and a seemingly rational explanation of the cause. Quoting from Raynaud's thesis for his doctor's degree—as translated by Barlow:

"I propose to demonstrate that there exists a variety of dry gangrene affecting the extremities which it is impossible to explain by vascular obliteration—a variety characterized by a remarkable tendency to symmetry—so that it always affects similar parts, the upper or lower limbs or four at the same time, further, in certain cases, the nose and ears; and I hope to prove that this kind of gangrene has its cause in a vice of innervation of the capillary vessels, which it remains for me to define."

Raynaud's second paper appeared in 1874. Munro of Glasgow wrote a monograph of the disease in 1899 which is a complete critical survey of the known facts of the disease to that time. Other articles appeared by Barlow and Cassirer.

(iii.) Aetiology. — (a) Nationality. The disease is said to be more common in England and France than in Germany. It is not rare in America. (b) Sex.—Women are much more frequently affected than men. Of Raynaud's 25 cases, 20 were women. Monro reports 62.5% in women. (c) Family Disposition.—Many incidences of several members of the same family being affected are reported, but no definite relation to heredity seems to exist. (d) Phychical Disturbances.—Onset of symptoms has been assigned to sudden shock or fright. Nervous, highly-strung persons are said to be more susceptible to the disease. (e) Cold.—Exposure to cold as in washing the hands in cold water is the usual exciting cause of an attack. It is obviously impossible to go on to a consideration of the pathology of the arteries as in the former two diseases, as Raymond described a condition in which there was no organic change in the arteries.

(iv.) The Nature of the Disease. Since Raynaud's publications and to the present day the general opinion as to the nature of this disease has been that there is a vasomotor instability probably as an increased irritability of the sympathetic vasoconstrictor fibres causing intermittent vascular spasm.

Osler, in giving a theoretical explanation of Raynaud's phenomena discusses the normal reaction of the skin vessels to cold and then goes on to the following delightful comparison: "There are persons in whom the centres controlling the vasomotor actions are unstable—the machinery of the irrigation centre is in charge of an inexperienced official who has not learned to work the sluices in proper response to the telephonic demands; he turns a full head of water on into one of Mr. Epidermus' farms and forgets all about it, or he shuts off all the supply from another, flooding the one, parching the other, and unless a call gets through in time to correct the mistake, death of crops is the result. This is exactly what happens in Raynaud's disease. The centres are at fault and working imperfectly." Such theories as these are, however, without experimental basis.

In 1925 Brown and others made observations with capillary microscopy confirming former theories as to the nature of the disease. Brown concluded from eight cases under various con-

ditious and in different stages of the disease, that in local syncope (pallor), there is a constriction of all the vascular elements of the skin, and that in local asphyxia (cyanosis), there is a refilling of dilating capillary loops.

In 1928 Sir Thos. Lewis made certain conclusions based on human experiments, some of which are quite convincing and to some extent contrary to general belief.

1. He states that the immediate cause of defective circulation in an attack involving the hands is spasm of the digital arteries, and that vessels of smaller calibre, and vessels on the venous side are not primarily involved in spasm

2. His experiments indicate that the abnormal spasm of a spontaneous attack is produced locally by some fault of the digital arteries and not by vasomotor nerve impulses. He anaesthetized the ulnar nerve (and presumably the sympathetic fibres with the same peripheral distribution) during an attack of local asphyxia in the little finger. This caused no rise in temperature and only slight change in colour. He reports that in cases which have had a sympathectomy performed for Raynaud's disease, with some relief, exposure of the extremity to cold produced the typical colour changes—but slightly less marked than before operation.

3. His conclusion is that the sympathetic nerves are concerned with the normal degree of spasm in the vessels, and not with the abnormal spasm which is due to a local fault in the vessels. Surgical intervention with release of normal spasm may be sufficient to give considerable relief.

More recently, Scott and Martin have made the same statement in regard to the role of the sympathetic nerves in this malady.

It is of interest to note that Raynaud includes mild cases manifesting only local colour (and temperature) changes, such as the condition called "dead finger," in his original description. Cases showing necrosis of tissues are classed as severe cases.

Lewis's investigations tend to disturb our preconceived idea as to the aetiology of this disease. One finds it difficult to so discount the role of the sympathetic nervous system, in view of many reported striking cures by sympathectomy. Simpson repeated these clinical experiments of local anaesthetization of all the sympathetic fibres which supply a finger completely abolished and prevented every manifestation of Raynaud's disease in that finger even in the most extreme conditions. Their results with severe and complicated cases were similar to those obtained by Lewis. They found that in severe cases, if all the sympathetic fibres were interrupted by anaesthetization, it was still possible for the digital arteries to enter into spasm with cyanosis. This, they attributed to secondary pathological changes in the arteries and arterioles. They point out that Lewis was working with severe and complicated cases. They state that the sweating which occurs during attacks, and the production of spasm by psychic factors, point to a sympathetic nerve disorder.

Spirling, Jelsima and Rogers attribute their failure to prevent gangrene in the fingers by sympathectomy in two cases, as probably due to a secondary vasomotor mechanism as suggested by Brauecher, rather than to a local fault of the arteries.

The weight of evidence at present seems to bear out Raynaud's original explanation of the disease as a vasomotor neurosis. Local disease of the arteries occurs in late cases.

In an editorial of the C.M.A.J. it is suggested that there is a family relationship between Pink Disease (Acrodynia). Raynaud's Disease, Chilblain and Erythromelalgia, with possibly a disorder of the sympathetic nervous system as a common denominator.

The most frequent lesion in severe cases is a "dry gangrene." It is sharply demarcated, and remains so until the

slough comes away Infections are rare and heal rapidly, resulting in a tapering cicatrix in the peripheral part. Moderately severe cases may show bleb formation with ulceration. Buerger describes atrophic changes in the bones in prolonged cases.

Cases of Raynaud's disease associated with scleroderma or even sclerodactylia have been reported (Matsui-Lewis) to show some intimal thickening in the digital arteries. These are old cases and it seems more likely that these organic vascular changes are secondary to prolonged spasm, than that the organic changes are primary.

SUMMARY.

1. A Clinical classification suggested by Brown, Allen, and Mahorner, is given for sake of completeness.
2. Two organic arterial diseases of the extremities have been considered, namely, arteriosclerosis and Buerger's disease — under the headings of: definition, aetiology and pathology.
3. The common lesion in arteriosclerosis of extremities is a destruction of media with degeneration and calcification, producing rigid inelastic arteries. Occulation is due to a secondary endarteritis with thrombosis
4. Thrombo angiitis occurs in a younger age group, and aetiological factors are different from arteriosclerosis The pathology of the lesion shows it to be essentially an inflammation extending from the adventitia to involve all costs of the arteriosclerosis are indicated. Cellular infiltration, vascular reaction, and perivascular fibrosis are prominent. The muscular media remains intact and calcification is absent.
5. Raynaud's disease has been considered as an example of the group classified as Functional or Vasomotor disorders. References are made to Raynaud's original theses, and more recent experimental work has been discussed.

ARTERIAL DISEASE OF THE EXTREMITIES

II. CLINICAL FEATURES.

By R. B. KERR, B.A., '33.

In this paper, discussion will be confined to the three important and most frequently encountered diseases of the arteries of extremities:

Thrombo-angiitis obliterans.
Arteriosclerosis.
Raynaud's Disease.

THROMBO-ANGIITIS OBLITERANS.

Buerger's Disease.

Thrombo-angiitis obliterans is an obliterative lesion of the deep arteries of the extremities, occurring more frequently in the lower limbs. It occurs entirely in men—there being but one known case in a woman The age incidence is from 25-40 years with exceptions to these limits.

Clinical Course.

About 75 per cent. of the cases of thrombo-angiitis obliterans fall into a type in which various manifestations occur in a more or less definite sequence during a period of from one to ten years. The occurrence of these manifestations may be divided into the following fairly definite stages:

1. Period of claudication, characterized by excessive fatigue and pain following exercise; associated with this are postural colour changes, that is, rubor on dependency and pallor on elevation of the limb.

2. Period of trophic changes, which is characterized by the appearance of non-healing ulcers, fissures and gan-

grene. Associated with these changes there arises a continuous severe pain.

Symptomatology.

Fatigue and claudication: The most frequent complaint at the onset of the disease is one of excessive fatigue of the muscles of the calfs, arch, ankle, or popliteal region of the affected leg, associated with cold feet This is followed by the appearance of the pain of claudication—this is at first a mild aching, following prolonged exercise, but soon progresses into a true cramping pain following ordinary exercise. Thus a patient will notice that as the disease progresses he will be able to walk a shorter distance before being forced to halt under the severe distress of claudication. The symptom of claudication is due to the decreased blood supply to the muscles of the leg. This may be demonstrated by the fact that if the arterial flow to a normal leg be occluded by means of a syhygmomanometer cuff a pain similar to claudication is produced following exercise.

Postural colour changes: This manifestation may appear at any time during the clinical course of the disease, but usually soon after the pain of claudication. When the extremity is elevated above the level of the heart in a normal person the normal colour is maintained. However, in the case of an extremity in which Buerger's disease exists, elevation produces a paling of the skin, whereas dependency of the affected part produces a marked reddish colouration or rubor which begins at the ends of the digit and spreads to involve the entire digits and lateral aspect and dorsum of the foot or hand. The colour of the part subsequently changes into a reddish cyanotic purple.

Trophic changes: Later in the disease trophic changes such as dystrophy of the nails, non-healing ulcers, fissures and cracks or dry gangrene appear. These appear most commonly on the outer or inner margin of the great toe, on the outer aspect of the small toe, or on the dorsum of the foot. These changes are frequently precipitated by surgical intervention in cases where the true condition is not recognized, by irritation such as tight shoes, blistering ointments and corn plasters, or by trauma. Gangrene frequently occurs as the disease progresses. It is of the dry type. The gangrenous area separates from the rest of the part.

Temperature changes: Early in the progress of the disease the surface of the affected members becomes considerably colder than normal. If the disease is unilateral there may be a difference of as much as 5 or 7 degrees C., between the affected and normal limbs.

Rest Pain: At some point in the progress of the disease, usually before the trophic changes appear, there is a distinct change in the character of the pain. Instead of being the intermittent claudication, the pain becomes continuous and progressively more severe. The pain typically occurs in the digits, on the dorsum of the foot, in the ankle or is limited to gangrenous areas. Some relief is obtained by heat and by the dependent position, while cold and elevation aggravate it. The pain may be sufficiently severe to prevent the patient from sleeping. Opiates have little effect upon the pain.

Various explanations of this pain have been put forward. Joblons attributes the pain to the fibrosis involving the nerves; Meleney and Miller believe that the pain is due to the obliteration of the nutrient vessels to the nerves; Putnam believes that a true neuritis is present; Allen and Brown suggest that it is due to the constant and prolonged anoxemia from which the tissues suffer. An interesting observation in this connection is that following sympathetic ganglionectomy this pain is relieved, whether this is due to the increase in the blood supply or due to the severance of pain tracts, is not clear.

Obliteration of arterial pulse: Pulsations of the dorsalis pedis, the posterior tibial or even the popliteal ar-

tery may be obliterated so that they are not palpable. This obliteration usually accompanies the appearance of the postural colour changes.

Phlebitis: (Migrating thrombophlebitis). Phlebitis occurs in about 40% of cases in the lower extremities and is rare in the upper extremities. The common site is over the main trunk of the internal saphenous vein and its branches below the knee. The picture presented is one of inflammation along the veins or in circular areas, termed cutaneous by Buerger. Sometimes segments of vein are removed at these points to prove an early diagnosis.

Oedema: Oedema occurs rather commonly in the lower extremities. It is probably due to thrombophlebitis of the deep veins and is accentuated by the dependent posture. Oedema is a serious complication in the presence of trophic changes, as it increases the danger of infection and decreases the speed of healing.

Sudden Arterial Occlusion: A sudden occlusion of the arteries may occur occasionally in Buerger's disease. This is accompanied by a sudden sharp pain in the foot, accompanied by extreme pallor and coldness The pain gradually subsides and has disappeared in 24 hours or longer. This manifestation not infrequently represents the first suggestion of disease and thus such a history should put one on guard for Buerger's disease if it occurs in a young adult.

Prognosis.

Early writers, as Perla and Buerger, give a very unfavourable outlook for the disease. From their accounts of the disease the affected limb is doomed to amputation in one or two years after the onset. However, due to a better understanding of the disease and more efficient methods of therapy, recent writers give a more optimistic prognosis. Allen and Brown conclude that in most of the cases the disease is self-limiting, since apparently the obliterating process eventually stops, and if the collateral circulation develops sufficiently the trophic changes disappear and the patient may be symptom-free for years or in some cases indefinitely. However, if in a limb there are trophic changes, accompanied by severe pain at rest, and infection with oedema, the probability is that the collateral circulation is poor or undeveloped and the limb will go on to gangrene.

There are several factors which influence the prognosis in any case. Early diagnosis and early institution of therapy to produce collateral circulation affects favourably the prognosis. The inability of the patient to take long periods of rest lessens the possibility of a satisfactory recovery.

To sum up the problem of prognosis it would be well to state that the outcome of the disease greatly depends upon the successful establishment of a collateral circulation sufficient to provide adequate blood supply to the part over the acute period of the obliterative process.

ARTERIOSCLEROSIS.

In arteriosclerosis proliferative changes and deposition of calcareous material in the walls of the vessels produce a loss of elasticity and diminution of the lumen of the vessels. These factors give rise to the clinical picture of impaired circulation, the picture presented depending upon the amount of circulatory impairment present. Arteriosclerosis is associated very frequently with the disease diabetes, so that the clinical picture of arteriosclerosis of the extremities is frequently a complication of that disease.

Clinical Course.

The course of arteriosclerosis of the extremities is one of gradual impairment of circulation. As the picture of this syndrome has been covered under the discussion of thrombo angiiitis obliterans no detailed description will be entered upon here. There are, however, some differences in the picture which are worth mentioning. First,

the onset of symptoms due to arteriosclerosis occurs at a later age than in thrombo-angiitis obliterans, above 60. The occurrence of ulcers and trophic changes are said not to occur as frequently with arteriosclerosis. Further, arteriosclerosis is frequently associated with diabetes.

Symptomatology.

The symptoms again are very similar to those already mentioned in connection with thrombo-angiitis obliterans. One manifestation, however, which is of value in connection with arteriosclerosis is the X-ray study. Roentgengrams of the affected limb show a density corresponding to the arteries when calcification has occurred in the arterial walls.

Prognosis.

The prognosis in senile arteriosclerosis if the limb has progressed to trophic change is not good due to the fact that the collateral circulation is involved in most cases as well. Amputation is usually necessary. In the early stages of the condition, with proper prophylactic care, the period of usefulness of the limb may be prolonged.

In diabetic arteriosclerosis the treatment of the diabetes with insulin does ont appear to have a very favourable effect upon the arteriosclerosis, for it appears to progress as far as is known now. Thus arteriosclerosis has become accountable for 50% of the deaths in diabetics.

RAYNAUD'S DISEASE.

This condition is a spastic lesion of the arteries of the extremities. The disease is relatively rare. It occurs much more frequently in women than inn men, between the ages of 18-40 years. The condition is said to occur more frequently in the upper extremities, and is not infrequently bilateral.

Clinical Course.

A description of a more or less typical case of Raynaud's disease is given as follows: A person from 18-40 years, usually a woman, suffers a more or less severe pain somewhere in the peripheral parts of the body. The pain is not confined to any distinct nerve distribution, but is usually bilateral. This is accompanied by (1) blanching of the part, (2) appearance o a bluish colour of the part, and (3) trophic changes progressing often to gangrene. The disease usually shows several attacks occurring in succession, between which there may be intervals which are completely free of attacks. Exposure to cold frequently initiates an attack.

Symptomatology.

Local Syncope: Refers to the sudden blanching of a part, usually fingers or toes. The pallor is sharply demarcated; there is a decrease in surface skin temperature of about 15-20°. The attacks are likely to be precipitated by exposure to cold, and last from a few minutes to a few hours. Following this attack of pallor, there is a sensation of numbness, tingling or coldness, with which is associated the second important characteristic—

Local Asphyxia: This manifestation occurs usually following the attack of local syncope. There is a local anoxemia of the part involved which causes the part to become bluish white, or even dark blue and purple in colour. The surface temperature is decreased, but not as markedly as in the syncope. Usually this condition disappears after some time; if, however, it persists, the skin becomes very black and desquamates. Pressure over the affected part obliterates the bluish coloration of the skin, and this does not reappear for some time. Following an attack of this condition there may be a period of hyperaemia, with increased pulsations, warmth, tingling and redness.

Trophic Changes: With persistent attacks of these phenomena, gangrene of the peripheral parts eventually results. There may appear on the finger sharply demarcated blackened areas, which remain dry and then separate; or there may appear blebs at the tip

of the finger which discharge a black sero sanguinous discharge, or there may be merely a thickening of the skin over the tip of the finger.

Pain: Pain almost constantly occurs in this disease. It usually coincides with the attack of syncope or asphyxia as a painful numbness which is followed by a sensation of burning and tingling.

Pulsations of Vessels: Many believed that pulsations of the dorsalis pedis artery or radial artery were absent during an attack, but this is now considered to be not true. The pulsations are diminished but may always be elicited.

Bone Changes: One or more of the terminal phalanges may atrophy and disappear. The long bones may show change as well; there has been recorded to be a thinning of the cortex and a narrowing of the marrow cavity in some instances.

Haemoglobinuria: There have been some few cases of Raynaud's disease which have shown haemoglobinuria; this is presumably due to the fact that some similar change occurs in the renal artery which damages the kidney.

Central Nervous System Manifestations: Osler mentions that attacks of Raynaud's disease have been observed in individuals suffering from various types of mental disorder. A few cases have been recorded in which transient, hemiplegias, asphasias or paraplegias have developed, in all probability due to changes in the vascular structures of the brain.

Prognosis.

In the past, prognosis has been very poor, and amputations have been performed frequently to alleviate pain. However, with earlier observations of cases and more satisfactory therapeutic measures it has been possible to offer a more hopeful prognosis and to maintain the usefulness of the affected part for many years.

Special Methods of Investigation.

1—**Rate of Blood Flow**: A method of measuring the rate of blood flow through an extremity is of extreme importance not only in arriving at an estimation of the extent of arterial occlusion in a given case, but in the observation of the effect of various therapeutic measures upon the restoration of circulation in the affected extremity. Stewart's calorimetric method as modified by Kegerreis has been used in this connection. In this method the extremity is immersed in water in a calorimeter, and the rise in temperature of the water gives an indication of the heat lost by the limb in given period. The loss of heat per unit area is very approximately inversely proportional to the blood flow through the limb. Thus in a case of Buerger's disease there is a marked decrease in the heat loss per unit area as compared with the normal.

2—**Methods of determining the possible increase in blood flow following nerve path interruption**: As will be mentioned later, it is important to know, before submitting the patient to ganglionectomy, the amount of increase in the rate of blood flow in the collateral circulation that can be expected following such procedure. To find this the following methods have been suggested:

(a) Spinal anaesthetic: It has been shown that during a spinal anaesthetic there is an increase in temperature of the limbs due to a dilatation of the vessels of the limb. This dilatation is resultant from the paralysis of the sympathetic fibres from the spinal cord by the novocaine. The skin temperature is measured by means of an electro-thermo couple.

(b) Recently Morton has suggested a further method — consisting of injecting novocaine into the vicinity of the posterior tibial nerve, and observing the effect upon the skin temperature following this procedure.

Of course, careful control must be kept of the room temperature during

these tests, so that the cooling due to the difference of temperature between the skin and the environment will be taken into account.

In an extremity in which ganglionectomy would produce a marked dilatation of the vessels of the limb, especially the collateral channels in a diseased limb, there will be an increase in skin temperature following the above procedures — indicating that a favourable result from ganglionectomy may be expected.

Treatment.

The methods of treatment of the three diseases discussed overlap to such an extent that it was considered advisable to deal with this phase in such a way as to more or less apply to them all. To begin with, a summary of the methods of treatment recommended for each condition will be given:

1. Thrombo-angiitis obliterans: as recommended by Allen and Brown.
   (1) Extensive gangrene — amputation.
   (2) Mild trophic changes with rest pain—
      (i) Promote circulation to heal ulcers, including lumbar ganglionectomy.
      (ii) Amputation if rest pain cannot be relieved.
      (iii) Prophylaxis.
   (3) Mild trophic changes without rest pain—
      (i) Promote circulation to heal ulcers, including lumbar ganglionectomy.
      (ii) Prophylaxis.
   (4) Severe rest pain with no trophic changes — as for (2).
   (5) No trophic changes and no rest pain—
      (i) Prophylaxis.
      (ii) Medical measures to increase circulation.
2. Arteriosclerosis:
   (1) Prophylaxis in mild cases.
   (2) Increase circulation to heal ulcers and in impending gangrene.
   (3) Amputation.
   (4) Treatment of diabetes.
   (5) Sympathectomy helps a few—10%.
3. Raynaud's Disease:
   (1) Prophylaxis in mild cases.
   (2) Sympathetic ganglionectomy.

A discussion will now be undertaken of the various methods of treatment suggested:

1—**Prophylaxis**: In early cases of arterial disease, and in recovered cases of Buerger's disease, care of the feet does much to save the limbs from severe trophic changes. The feet should be washed often with soap and water to keep them soft and free of scales. Nails

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should be softened with lanolin and trimmed so as not to injure the toe. Tight stiff shoes should not be worn; corns should be trimmed only with care; trauma should be prevented. Exposure to cold should be prevented by the wearing of heavy hose and shoes. Surgical procedures, such as toe-nail removal, should be condemned. Cessation of smoking in Buerger's disease is indicated as valuable.

2—**Methods of increasing the circulation:** The value of increasing the collateral circulation, especially in thrombo-angiitis obliterous, has already been referred to. Such a procedure, if possible, will carry the patient over the acute obliterating process of the disease in many cases.

(a) MEDICAL—(1) Postural exercises—Buerger introduced this means of stimulating collateral circulation. The exercises are carried out by elevating the extremities perpendicular to the bed for one minute and hanging them over the bed for one minute. Repeated for three 15-minute or longer periods a day. The alternate emptying and filling of the collateral vessels produced by this procedure is beneficial in the opening of the collateral circulation.

(ii) Contrast Baths—This procedure consists in alternately immersing the extremity in warm and cold water for one minute each for 15-minute periods three times a day. The warm water is 100-110° F., and the cold water 40-50° F. This procedure produces an alternate contraction and relaxation of the collateral vessels.

(iii) Radiant heat—In the form of electric cradles is of considerable value in producing an increase in the circulation provided that provision is taken not to allow the part to suffer a burn.

(iv.) Non-specific protein—Injections of the triple typhoid vaccine beginning with doses of 20-50 million and increasing up to 300 million, have been tried and are found to be very successful both in relieving pain and in increasing the blood supply to the part.

(v.) Intravenous administrations of solutions—Various attempts to administer such solutions as isotonic sodium chloride, Ringer's solution, and sodium citrate solutions have been made with a view to reducing the tendency to thrombosis. However, the results of such procedures are not conclusive.

(b) GANGLIONECTOMY—In Raynaud's disease the condition is believeed to be due almost entirely to a spasm caused by a nervous imbalance in the controlling mechanism of the arteries. Thus if this imbalance is removed beneficial results will occur. The thrombo-angiitis obliterans there is a spasm of the collateral vessel believed to be caused by a nervous reflex from the inflamed areas. Thus in this latter disease removal of that spasm will result in beneficial effects as far as the establishment of a collateral circulation is concerned, dependent upon the degree of spasm present. The efficacy of interference with the nervous mechanism can be estimated by procedures outlined above with the aid of a spinal anaesthetic. In arteriosclerosis interference with the nervous mechanism is of doubtful value, but if it could be selected accurately a few might be saved.

Leriche first introduced the surgical method of periarterial sympathectomy, by which he stripped the adventitia from the larger vessels believing that wtih this he removed the sympathetic nerve supply to the vessels of that limb. He obtained a transient vasodilatation. Later the procedure of ramisection or ganglionectomy, i.e., obliteration of the sympathetic ganglia of the region involved, was introduced chiefly by Allen and Brown. This procedure produces a more prolonged vaso-dilatation, and probably represents the most efficacious measure of therapy in selected cases.

3. **Amputation:** In thrombo-angiitis obliterans, it has been recognized that amputation need not be undertaken as early in the disease as was formerly thought, nor need it be as radical. Ex-

cept in cases of extensive gangrene, conservative treatments are to be recommended. Most authorities recommend that the limb be left until a definite demarcation is formed, and then amputate as low as can be done, hoping for the re-establishment of the collateral circulation. The financial position of the patient, however, greatly influences the procedure in regard to amputation. If it is not possible for the patient to undergo extensive and costly treatment, it is perhaps advisable to amputate high and early.

In arteriosclerosis, high amputation will have to be resorted to eventually. It is advisable to extend the height of amputation until free bleeding occurs. In diabetic patients it is well to attempt to control the diabetes before beginning operative procedures.

In Raynaud's disease amputation is indicated only if there is extensive gangrene present.

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M.D., Waco, Texas.

J.A.M.A., *Dec. 19, 1931*, *p. 1914*

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